OBSERVATIONS UPON APPENDICITIS.

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[CONTINUED FROM PAGE 362.]

BACTERIOLOGICAL CONSIDERATIONS.

THE question of the relation existing between the bacteria of the intestinal canal and the etiology of appendicitis has recently awakened an unusual interest among both bacteriologists and surgeons, owing to a more careful study of these micro-organisms. From the time when the digestive tube becomes the receptacle of food and its products, these bacteria are found in greater or lesser variety.

Attention has been particularly called to the ordinary and common form of bacillus which is found in the discharges from the intestinal canal so constantly that the latter has come to be looked upon as its natural habitat. This organism, known as the *bacillus coli communis* (Escherich), it would appear, bears a more or less definite relation not only to inflammatory conditions within the abdominal and pelvic cavities, but likewise to these conditions when occurring under certain circumstances remote from the intestinal tract. For instance, it may, according to a number of observers, pass the barrier of the intestinal mucosa, although under favorable conditions it is claimed that it may even give rise to active desquamative lesions here, and penetrate into the general circulation; thus reaching parts remote from its original and apparently normal location, in which it seems to play an innocent rôle; it has been claimed to give rise to suppurative conditions of the most decided character.

While the fact of its discovery in pure culture, in cases of enlarged spleen (Wyss), in a hæmatoma following thyroidectomy (Tavel), in diseases of the biliary passages Gilbert, Girode, Naunnyn), in abscess of the liver (Rodet, Veillon, Jayle, Stern, and A. Fränkel), in lymphangitis of the arm (Levy), in septic emphysema (Chiari), in general pyæmic infection, with suppurative meningitis (Stern), and in broncho-pneumonia, endocarditis, meningitis, nephritis, and cystitis (Henkemans), is of interest, yet its presence in connection with these conditions does not possess an importance beyond the fact that it serves to establish its migratory character in connection with our present study. Its presence in connection with suppurative peritonitis (Lamele, Reux, Rodet, and A. Fränkel) and in peritonitis consecutive to an intestinal lesion without perforation (Welch), and in cases of appendicitis, both acute, perforative, and chronic relapsing (Ekehorn, Roswell, Park, Hodenpyl), together with my own heretofore published observations upon this subject,[1] seem, at first glance, to establish a direct and specific etiological relation between the *bacillus coli communis* and inflammatory diseases of the appendix vermiformis.

In addition to demonstrating the existence of this micro-organism in the exudate of the accompanying peritonitis of appendicitis, it has been shown (Hodenpyl) that the cavity of the appendix in new-born children, as well as the healthy peritoneal cavity in general, is sterile. Again, in so far as experimental bacteriology can establish the fact, the *bacillus coli communis* has been demonstrated to be pathogenic to rabbits and guinea-pigs, when bouillon cultures made from isolated colonies, obtained from appendicitis cases, are injected into the abdominal cavities of these animals (Ekehorn, Hodenpyl, Wilson). The suggestion of Ekehorn,[2] however, that, in comparatively mild forms of the disease (recurrent and relapsing cases), the virulency of the bacillus is not so great as shown by its effects upon the lower animals following inoculation with cultures derived from acute and rapidly-progressive instances of the disease, is not borne out

[1] The New York Medical Journal, Vol. LVIII, October 14, 1893, page 434.

[2] Bacterium Coli Commune, en orsak till Appendicit, Upsula Läkere. Förh., 1892–3, XVIII, 113–150.

by experiments made for me by Dr. Wilson, at the Hoagland Laboratory, an account of which will be given on page 479.

The fact that the *bacillus coli communis* can be obtained in pure culture from the peritoneal surface of an inflamed appendix which has not undergone perforation, as well as from the walls of the organ, the interior of its mucous canal, from the contents of an appendicular abscess, and both isolated and non-encysted intra-peritoneal collections of fluid which have undergone changes the result of septic influences, is now well established. It has, likewise, been conclusively shown (Hodenpyl) that this micro-organism exists under normal conditions in the cavity of the vermiform appendix.

In one of my cases of appendicitis a pure culture of the *bacillus coli communis* was obtained from a layer of plastic lymph which glued the inflamed appendix to the cæcum. The mucous membrane of the organ was not involved in the inflammation, and, although the walls of the organ were involved in an exudative inflammatory process, a large number of sections made by Professor Van Cott failed to reveal the presence of the micro-organism. It will probably be found that decided disturbances of the relations of the intestinal canal, such, for instance, as the fixing of the colon in an abdominal wound for the purpose of an artificial anus, will lead to the migration of the intestinal micro-organisms. Dr. Bristow reports to me that in a case of this kind, occurring in his service at the Kings County Hospital, a pure culture of the *bacillus coli communis* was obtained from the exudate which formed between the serous surface of the colon and the parietal peritoneum. No sutures were employed in the case, the colon being simply lifted into the abdominal wound and there supported upon a glass rod. The cultures were taken on the third day following the first stage of the operation, and prior to the opening of the gut.

The assumption, however, that the *bacillus coli communis* is the sole infecting agent of appendicitis and perforative peritonitis is apparently unwarranted, according to Barbacci, of Florence.[1]

[1] Ueber Aetiologie und pathogenese der Peritonitis durch Perforation. Centralblatt f. Allgemeine Pathologie u. Pathologische Anatomie, October, 1893.

This observer examined 14 cases of perforative peritonitis in man, and made a number of experiments upon animals. Of the 14 cases, 1 was an aspirated so-called perityphlitic abscess; 7 were typhoid perforations; 2 were perforating ulcers of the stomach; 1 of perforation of the vermiform appendix; 1 of perforation from strangulated hernia; 1 of perforating ulcer of the cæcum; and 1 of gangrene and perforation following volvulus. Bacteriological examinations were made under favorable conditions,—*i.e.*, immediate autopsies in cold weather, to exclude putrefactive organisms.

Barbacci reaches the following conclusions:

(1) In perforative peritonitis in man, cultures from the exudate yield only one organism in the vast majority of cases,—the *bacillus coli communis*. In but a single case of the fourteen was another microorganism, the *micrococcus lanceolatus* (Fränkel), associated with the *bacillus coli communis*. (2) Inoculations into the peritoneal cavity of susceptible animals (white mice and guinea-pigs) with fresh exudate of peritonitis produce peritonitis, and in eight cases out of the thirteen the *micrococcus lanceolatus* was found. (3) The *micrococcus lanceolatus* is present in about 60 per cent. of all cases, but is overlooked because it is overgrown by the *bacillus coli communis*. (4) Experiments on dogs by opening the abdomen, securing a loop of intestine, and causing a perforation by the application of caustic potash produced a peritonitis exactly simulating, both microscopically and bacteriologically, a perforative peritonitis in man. The animals died in from twenty to thirty hours, and examination after death show a general fibrinous peritonitis. Enteritis was not found in any of the cases. Pure cultures of the *bacillus coli communis* were obtained from the exudate. (5) Marked differences exist as to the result when, upon the one hand, the examination is made directly from the exudate, or by the culture method, on the other. Cultures show only *bacillus coli communis*, but by direct examination a number of different organisms may be found, the latter dying in the exudate in the early stages of the inflammation, the *bacillus coli communis* growing alone in the cultures. In dogs killed at intervals of 5, 5½, 6, 8 and 10 hours after perforation, examination showed the *bacillus coli communis* mixed with other organisms up to eight hours; after this the former alone was found. The *micrococcus lanceolatus* was not found in the experimental peritonitis in dogs.

Dr. Ezra H. Wilson, pathologist to St. Mary's Hospital, director of the Hoagland Laboratory and chief of the Bacteriological Bureau of the Brooklyn Board of Health, at my request made bacteriological examinations in the following cases of appendicitis occurring in my hospital services. The operations for the removal of the appendix were conducted aseptically,—*i.e.*, only heat-sterilized instruments, etc., were employed; no antiseptic agents were employed in the case until after the removal of the organ. In each case the latter was ligated at two points, and the section for its removal made between two heat-sterilized ligatures. The appendix was then placed in a sterilized glass tube, which was immediately sealed and forwarded to the laboratory for examination. In two cases (Nos. 7 and 8) smear preparations for direct examinations, and direct cultures were also made.

The technique of the examinations was as follows: The cultures were made in peptone bouillon from the mucous membrane through sterilized incisions in the wall of the appendix. Cultures were also made from the outside of the appendix, and also from the exudate of the peritoneal cavity in some cases, at the time of the operation. Smear preparations were made directly from the exudate; these were stained and examined immediately.

Bouillon cultures were incubated for twenty-four hours and then plated. From the isolated colonies of the plated preparations other bouillon cultures were made, which were used for experiments upon animals.

The media employed were beef-peptone bouillon and gelatin.

CASE I.—November 7, 1893. Male, twenty-seven. No previous attacks. Was attacked suddenly with acute abdominal pain. Tumor developed rapidly, and was distinctly felt at the end of twenty-nine hours. Operation thirty-two hours after commencement of symptoms. Appendix surrounded by a mass of adhesions, and the seat of a cystic dilatation. No other adhesions. Appendix amputated between two ligatures and placed in a sterilized glass tube for examination. Recovery.

Bacteriological Examination.—Appendix surrounded by considerable new tissue and fibrin. Two cavities were present, separated by a constriction.

The lower cavity contained pus. Cultures were made from both cavities and from the outside of the appendix, and carried along parallel. The cultures from both developed pure *bacillus coli communis.* From 1 to 2 c.c. of bouillon cultures derived from isolated colonies were injected into the peritoneal cavities of guinea-pigs. The animals died in from twenty-four to forty-eight hours, and the organism was recovered in pure culture from the peritoneal cavity. It was not found in or recovered from the blood or organs. The peritoneal infection was very slight; the animals apparently died from general sepsis.

CASE II.—November 25, 1893. Male, fourteen. No previous attack. Suddenly attacked with usual symptoms; local tenderness developed within two hours. Fever pronounced from the commencement. No tumor. Operation on second day of disease. Appendix divided between two ligatures and removed. No perforation. Placed in sterilized tube as in Case I.

Bacteriological Examination.—Same technique as in No. I. Result; Pure cultures of *bacillus coli communis* obtained in all of the cultures. Pathogenic to guinea-pigs.

CASE III.—November 26, 1893. Male, twenty-eight. Two previous attacks; the first two years, and the second one year, ago. Present attack sudden in onset, with general abdominal pain. Temperature ranged from 101° to 102° F. No tumor. Great prostration and anxious facial expression from the second day. Admitted to hospital on the fifth day, and operated upon at once. Sero-purulent fluid in the peritoneal cavity. Appendix removed and cared for as in other cases. Appendix gangrenous, perforated in two places. Three small fæcal masses present. Patient died of profound septic intoxication and pre-existing peritonitis in thirty-six hours.

Bacteriological Examination.—Technique same as in Nos. I and II. In the Petri dish colonies of a different nature were found. These proved to be the *bacillus pyogenes fœtidis.* The colonies of *bacillus coli communis* were scanty, while those of the *bacillus pyogenes fœtidis* were very abundant.

The *bacillus coli communis* was pathogenic for guinea-pigs, causing death in forty-eight hours. The death resulted from peritonitis and toxæmia combined.

The *bacillus pyogenes fœtidis* proved to be exceedingly virulent. It was pathogenic for guinea-pigs when used in the same manner as the *bacillus coli communis,* causing death of the animal in twelve hours.

Bouillon cultures derived from isolated colonies of the *bacillus pyogenes fœtidis* were filtered through sterilized Chamberland filters, and proved to be sterile of culture. Two c.c. of this sterilized culture were injected into the abdominal cavity of guinea-pigs with a negative result. The animals recovered in each instance.

CASE IV.—November 28, 1893. Male, twenty-two. Chronic relapsing appendicitis operated upon one week following a relapse. First attack five months previously; has suffered one attack each month on an average since. No tumor. Appendix thickened, surrounded by slight adhesions, and hanging from its implantation in the cæcum in the shape of an inverted interrogation point.

Bacteriological Examination.—Cultures made from the outside of the appendix and from the exudate. Both developed pure *bacillus coli communis.* Bouillon cultures twenty-four hours old made from isolated colonies were injected into the peritoneal cavity of guinea-pigs. These caused death in thirty hours. The organism was recovered pure from the peritoneal exudate, but not from the blood or organs.

CASE V.—December 7, 1893. Male, ten. Chronic relapsing appendicitis operated upon one month following the fourth relapse. Patient also the subject of acromegalia. No tumor. Typical amputation of the appendix, which was four and a half inches long, corkscrew-shaped, placed in the directly downward (*S*) position, and notably thickened.

Bacteriological Examination.—Cultures from the appendix and its cavity developed from *bacillus coli communis.* Pathogenesis not tested.

CASE VI.—December 11, 1893. Male, twenty-four. One previous attack eight years ago, which led to the formation of abscess. This was incised. No attempt was made to remove the appendix at that time. Present attack sudden in its onset, and accompanied by the usual symptoms of an average severe attack. Chill occurred on the third day. Pneumonia developed and present at the time of the operation. Tumor present. Lumbar tenderness. Operation between the fourth and fifth day. Appendix found to be entirely extraperitoneal. Removed. The patient made a good recovery in spite of the presence of pneumonia at the time of the operation.

Bacteriological Examination.—A mixed growth developed, consisting of a micrococcus and a bacillus. The latter was rather larger than the *bacillus coli communis*, and stained very slowly. The micro-

coccus was somewhat larger than the *staphylococcus pyogenes aureus*, and stained readily. Placed in Petri dishes and isolated, the micrococcus proved to be the *micrococcus flavus aquefaciens*, and was evidently a contamination. The bacillus proved to be *bacillus coli communis*.

CASE VII.—December 15, 1893. Male, twenty-three. Four previous attacks at intervals of about a year. Present attack came on gradually for first twenty-four hours. It then suddenly developed into an acute condition, following which septic symptoms and great prostration rapidly supervened. Abdominal cavity, upon being opened, revealed some clear fluid. Some of this was obtained in sterilized Sternberg bulbs. A large sero-purulent collection surrounded the appendix. Smear preparations were made on clean slides directly from the exudate. Cultures upon agar plates were also made directly from the exudate. Appendix removed and placed in a sterilized glass tube. Patient died in thirty-six hours from profound sepsis.

Bacteriological Examination.—The smear preparations show a variety of organisms. Small diplococci resembling the *diplococcus lanceolatus*, small and large bacilli, some of which resembled *bacillus coli communis*, and a streptococcus resembling the *streptococcus pyogenes* were present. Single colonies from one agar plate, at room temperature for twenty-four hours, show pure *bacillus coli communis*. The other agar plate, placed for the same length of time at incubating temperature, showed likewise only *bacillus coli communis*. The serum drawn from the peritoneal cavity in the Sternberg bulbs before opening the encysted sero-purulent collection was found to be sterile.

CASE VIII.—December 20, 1893. Male, twenty-one. No previous attacks. Present attack developed suddenly, with usual symptoms of an average severe case. Fever present from the commencement. Appendix found surrounded by adhesions and considerable sero-purulent fluid. Cavity of peritoneum well walled off. Smear preparations made directly from the exudate, and obtained some of the exudate directly with sterilized Sternberg bulbs. Appendix removed, ulcerated and perforated. Placed in sterilized glass tube. Recovery.

Bacteriological Examination.—Cultures made from the exudate on slanting agar, and from the exterior and interior of the organ all developed pure *bacillus coli communis*. The smear preparations show the same variety of organisms as the preceding case,—*i.e.*, a diplococcus, the *diplococcus lanceolatus*, a bacillus, the *bacillus coli communis*, and a streptococcus, probably the *streptococcus pyogenes*.

CASE IX.—December 25, 1893. Male, seventeen. Chronic relapsing appendicitis operated upon in an acute relapse. Present attack came on ten days previous to admission to the hospital. Fever present since that time. Tumor present. Appendix found embedded in a mass of inflammatory adhesions. Smear preparations made. Appendix removed.

Bacteriological Examination.—Cultures made as before. Result, pure *bacillus coli communis.*

CASE X.—December 25, 1893. Female, twenty-one. No previous attack. Present attack sudden and accompanied by usual symptoms. Fever from commencement of the attack. Appendix infiltrated. No adhesions. No perforation. Recovery.

Bacteriological Examination.—Pure cultures of *bacillus coli communis* obtained from walls and interior of appendix.

CONCLUSIONS.

(1) The *bacillus coli communis* exists constantly in the lumen of the appendix and also in the exudate in the peritonitis accompanying inflammations of that organ. This can be demonstrated both by direct examination and by cultures.

(2) Other bacteria than the *bacillus coli communis* exist constantly in the exudate, and can be demonstrated by direct examination, but very rarely by culture.

(3) That perforative peritonitis from appendicitis is not a mono- but a poly-infection, and that, while the *bacillus coli communis* probably has the largest share in the infection, the presence of other organisms cannot be ignored.

THE PATHOLOGICAL ANATOMY OF THE APPENDIX VERMIFORMIS.

Two great classes of facts must always form the basis of knowledge concerning the diseases of an organ or part,—*i. e.*, first the anatomy, gross and microscopic, and the physiology of the part; second, the general pathological laws governing tissue lesions.

As has been already shown, the vermiform appendix is in effect a diverticulum from the caput coli, and retains, to a great extent at least, the structure of this portion of the larger intestine. Its exact location has been fully described in the section upon

the anatomy of the organ. In this connection, however, it will be convenient to review some of the prominent points in connection with its morphology.

The vermiform appendix is possessed of four coats: (1) A serosa, continuous with and resembling that of the caput coli; (2) a muscularis, composed of (*a*) an outer sheath of longitudinal fibres, and (*b*) an inner sheath of circularly-placed fibres. The last named is rather the thicker layer of the two, but the first partakes more decidedly of muscle of the character of non-striated variety; the muscle-tissue present in the circular layer is also of the non-striated type; (3) a submucosa, similar to the general submucosa of the intestinal canal; (4) a mucosa propria, resembling that of the larger intestine, with the exception that it contains quite constantly solitary lymph follicles in varying numbers. These latter may also be present in the submucosa.

The histology of these four tunics is identical with that of the larger intestine, with the two exceptions of the greater constancy of the solitary lymph-nodes in the mucosa and the complete outer sheath of longitudinal fibres in the muscularis.

The appendix is rich in minute blood-vessels, lymphatics, and nerves, the latter being the plexus of Meissner and Auerbach. The organ is usually supplied with a meso-appendix which assumes the shape of a triangular web, having one free and two attached borders. This membrane forms the stroma supporting the vascular and nervous supply to the part. It often contains considerable adipose tissue, and sometimes lymphatic glands.

The circulation in the appendix is practically a terminal one, the great volume of blood passing to it through a single vessel; only slight collateral circulation being derived through continuity of structure with the caput coli. In the female a third source of supply is found in the appendiculo-ovarian ligament, which carries a vessel to the appendix. Lymphatic channels are distributed throughout the meso-appendix.

Relatively large nerves also course with the blood-vessels, and must be regarded as motor, sensory, and trophic. In an experiment conducted at the Hoagland Laboratory by Professor Van Cott, stimulation of the nerve supplying this part in a dog

was followed immediately by a spasm of the muscular structure, very much resembling an erection of the penis.

One more circumstance in the anatomy of the appendix, more fully treated of in another section, may be mentioned here, —*i.e.*, that the blind or distal end of the organ has normally no attachment, thus permitting free motion of the part.

Physiologically the extent of the function of the appendix is to secrete mucus. In addition to this it is capable of peristaltic movements, to a greater or lesser extent, varying with the relative proportions of its longitudinal muscular coat and its circular fibres. These cover the ground, in this respect, as far as our knowledge extends at this time.

With this review and classification of such facts concerning the organ as are at present available to us, it becomes certain that this part of the anatomy must be subject to the same great pathological laws which govern all tissues; so that it may be logically concluded that certain pathological conditions obtain here as elsewhere, and are susceptible of classification according to a definite system. Lesions of the appendix may be thus described:

(1) Hyperplasia. General anomalies of formation.
(2) Circulation disturbances; oligæmia; hyperæmia.
(3) Non-specific inflammation
  (*a*) Catarrhal.
  (*b*) Purulent.
  (*c*) Fibrinous.
  (*d*) Combinations of *a*, *b*, and *c*.
  (*e*) Interstitial.
(4) Specific inflammation
  (*a*) Tubercular.
  (*b*) Typhoid.
(5) Progressive nutrition disturbances
  (*a*) Consecutive hyperplasia of any or all of the tunics.
  (*b*) Neoplasms
    Carcinoma.
    Endothelioma.
    Sarcoma.

(6) Regressive nutrition disturbances: atrophic changes involving any or all the coats from deficient vascular or nervous supply.
(7) Foreign bodies: such as enteroliths and accidental substances.
(8) Parasites: the various intestinal micro-organisms.

That all of these various conditions do exist in the appendix has been repeatedly shown by many investigators. Each exam-

ination of the specimens derived from a series of appendicitis cases from my own clinics, made by Professor Van Cott, demonstrates many of the varieties of lesions in the above enumeration.

The one point of keenest interest in the pathology of the appendix is involved in the answer to the question, Why, if this portion of the intestinal tube corresponds so closely to the remainder of the alimentary canal, is it so much more frequently the seat of lesions than any other portion of the tube? Or, to express it in another way, Why, if the same pathological laws govern the tissues of the appendix that govern the other tissues of the body, do they assert themselves so much more frequently here than elsewhere?

There is one prime factor which, more than any other, is responsible for this fact,—to wit, that here, as nowhere else, certainly in the abdominal cavity the parts are peculiarly exposed to circulatory, and hence to nutritive disturbances. Professor Van Cott's careful examination of my specimens furnishes convincing proof that vascular and nervous lesions are potent factors to ultimate disease of the appendix. In addition to this, proof is furnished by the interesting fact that females are less frequently stricken with the disease than males; and that, as already stated, in the female sex an extra supply of blood is furnished to the appendix through the medium of the appendiculo-ovarian ligament, a fact bearing directly upon the question of nutrition.

In all of the specimens subjected to examination, thirteen in number, there was revealed the presence in the mesenteric vessels of some form or other of obstruction to the blood-current, either endovasculitis or organized thrombus, conditions which must, in the nature of the case, have long preceded the intense small round-cell infiltration, the coagulation necrosis, and purulent foci present in the walls of the appendices themselves. In several cases, in addition, a distinct neuritis interstitialis chronica supervened; in one, the hyperplastic endo- and perineurium being so abundant as to have caused extensive atrophy of the nerve-fibres.

It is indisputable that such lesions of vessels and nerves can

only result ultimately in a most profound disturbance of the appendical tissues, with lessened resistance and localized necrosis. Why the appendix, for example, should be free from the consequences of anæmic infarct, so certain in the renal and other tissues endowed with a terminal circulation, is difficult to comprehend. On the other hand, if the trophic fibres, which must exist in the nerves of the meso-appendix, be subjected to pressure through hyperplasia of their connective-tissue sheaths to the extent of causing atrophy, trophic changes must necessarily occur in the appendix itself, and will be co-extensive with the nerve lesion.

The results of vascular obstruction are directly analogous to ulcus ventriculi, dependent upon endarteritis of the gastric vessels; those of trophic nerve lesions to perforatory ulcer due to trophic nerve lesions of an extremity.

It has been already shown that the great mobility of the appendix and its mesentery render these structures liable to torsion, and it can scarcely be doubted that this stands in direct etiological relation with the vascular and nervous degeneration.

Assuming the correctness of these conclusions, it is evident that two things are possible: (1) That the real cause of the *locus minoris resistentiæ*, which admits of bacterial infection of the appendix, must be sought, not in trauma of the mucosa, but rather in trophic disturbances of the appendix resulting from (*a*) chronic vascular lesion, (*b*) chronic nervous lesion, or (*c*) both of these combined; and (2) that this trophic disturbance will be intense or moderate, depending upon the nature of these lesions. Hence, it must follow, that ulcerative processes in the appendix, while they may be increased by bacterial invasion, may, nevertheless, owe their origin to the trophic conditions. Therefore, it must always be difficult to prove that a given ulcerating process, or pus-focus in the appendix, is due to bacterial invasion primarily; and the more especially is this true when lesions of the vessels and nerves of the mesentery obtains. It would seem much more cogent reasoning to assume that bacterial invasions were made possible by the lessened resistance of the part through defective nutrition than that primary necrosis is the result of direct invasion of germs through a normal mucosa.

Reasoning from the findings in the group of specimens of diseased appendices, furnished from my own operative work, already alluded to, another source of trophic disturbances would seem to be in progressive hyperplasia of the coats of the appendix, probably due to repeated hyperæmia or chronic stasis through defective venous return.

It is not to be denied that other causes are operative in producing necrosis of the mucosa, with consequent infection, as, *e.g.*, angulation of the appendix, the presence of foreign bodies in the lumen of the parts (a very rare circumstance, however), enteroliths, etc. It may be definitely stated in this connection, however, that all efforts to establish the existence of a specific bacterium which is responsible for appendicitis have failed; and it is now known that when microbic infection occurs, it may be simple or mixed, and that several varieties of organisms may find their way into the peritoneal exudate at once. This goes far to prove the presence of other etiological causes than micro-organisms; this, in its turn, strengthens the assumption that the local disturbances of tissue-nutrition and resistance are operative to the production of the inflammation.

Consideration of the so-called chronic relapsing cases of appendicitis throw additional light upon the whole subject, not only in its pathology, but also in the practical deductions which should aid the surgeon in his decision regarding operative interference. The cases now under consideration behave in a manner entirely consistent with the macroscopic and microscopic findings. The meso-appendix is hyperplastic, and so also is the appendix itself the seat, in many instances, of progressive hyperplasia. Everywhere, in the specimens derived from this class of cases were found new-formed connective tissue; and the vessels regularly show hyperplastic changes involving sometimes all and sometimes one or two of their coats. The same lesions are observed in the nerves. Similar lesions in the liver or kidneys would be called cirrhosis. With the lapse of time there is a general tendency to progression, until, finally, that which was at first too slight to give much semeiology suddenly asserts itself with an explosion of pain, marked reflex symptoms, vomiting,

etc., followed by temperature-symptoms and other evidences of sepsis. It cannot be certainly said at just what period of the existence of the conditions present infection first occurs. That this is true is shown by the clinical fact that fever and other evidences of infection are not present in the first few hours of the attack; abundant analogy goes to show, however, that the pain, which, without exception, ushers in the attack, as well as the muscular spasm, are the direct result of the progressive nerve lesion. Admitting that these lesions do not exist primarily in the meso-appendix, it never can be known just when the trophic disturbances are to result in necrosis of some area of the mucosa; nor can the extent of the necrosis be estimated. The practical conclusion to be drawn from this is that, with the first attack, with the diagnosis reasonably certain, it may be definitely stated that a condition is at hand which may at any time assume most threatening proportions, and which must eventually result in disaster. It is entirely within reason to suppose, from this view of the subject, that small areas of the mucosa may from time to time become thus necrosed, and local infection result. What is to follow such a process will depend upon two facts: (1) The amount of resistance in the appendix as a whole,—*i. e.*, the general condition of its blood-supply, etc.; and (2) the potential energy or virulence of such parasites as may happen to be lurking in the lumen of the appendix at the time. It is obvious that these two points can scarcely be determined *intra vitam* with any certainty, for the reason that such clinical symptoms as pain and fever are by no means in constant ratio with the extent of lesion. From this the deduction follows that, after the first attack, an individual smitten with this form of appendicitis is never safe; and in this connection it should be remembered that during such attacks adhesions may be formed which not only tend to increase the lesion in the meso-appendix, but may very seriously modify the operative possibilities. From this point of view, as well as from every other consideration founded upon our present knowledge of the disease as a whole, it is far more logical to proceed at once, under proper aseptic and antiseptic precautions and skilful technique, to remove the appendix, thus avoiding the con-

stant danger of fatal general infection, on the one hand, and serious difficulty in removing the appendix itself because of delayed operative interference, on the other.

Of the circulatory disturbances in the appendix it may be further said that oligæmia will supervene where progressive obliterating endarteritis is at hand, or where torsion is severe, or where a foreign body is present in the lumen of the tube; while hyperæmia may originate either from torsion upon the vein or, secondarily, as a result of local infection. Both conditions may undoubtedly obtain as a result of nerve lesion. That these conditions may produce effects upon the vitality and resistance of the appendix has already been shown.

In speaking of non-specific inflammation, it is not intended in this connection to convey the idea that bacteria plays no rôle in the process, for it is beyond dispute that they always do. The point here lies in the effort to discriminate between appendicitis resulting from such organisms as tubercle bacilli and those forms of the disease in which several pyogenic organisms seem equally competent to produce the inflammatory condition, and do so in conjunction with the trophic changes.

Summing up all the facts at our command, it is evident,—

(1) That appendicitis results primarily from circulatory and nervous disturbances which greatly lower the resistance of the part; and that the vascular and nervous disturbances are due either to immediate torsion of the meso-appendix or chronic progressive hyperplasia of the same.

(2) That the nature of the inflammation in the given case will be, (*a*) catarrhal, (*b*) purulent, (*c*) fibrinous, (*d*) a combination of the above named, or (*e*) interstitial. These, in turn, will depend upon the degree of circulatory and nervous disturbance, and upon the nature of the micro-organisms present.

(3) It can now be certainly shown that, in the given case of acute appendicitis, this initial attack is resultant from sudden torsion, and is not the first warning of a chronic infective meso-appendicitis, with progressive trophic lesions of the appendix.

(4) Weighing the chances of general infection of the peri-

Plate II.

Fig I

Fig II

Fig III

Fig IV

toneum, or of the system at large, engendered by delay, with those of infection from a properly-conducted operation, the decision, from a pathological stand-point, must be in favor of early operation.

Of the pathological anatomy of the appendix, aside from inflammation, there are a few points of diagnostic value.

The nature of certain progressive and regressive nutritive disturbances has already been discussed. Of the neoplasms, it is to be remembered that carcinoma, endothelioma, and sarcoma have been observed. While there have been too few cases on record as yet for statistical purposes, the possibility of a real neoplasm must always be a factor in the diagnosis of appendicitis.

Of foreign bodies popularly supposed to find entrance into the appendix, it is generally admitted that this only seldom occurs. Fæcal impactions are more common, but even these are only present in a relatively small number of cases.

[TO BE CONTINUED.]

PLATE II.

ILLUSTRATING SOME OF THE CHANGES OBSERVED IN ACUTE APPENDICITIS.[1]

FIG. 1.—Acute and rapidly progressive appendicitis, with gangrene and perforation.

FIG. 2.—Interior of the same; the mucous membrane of the appendix at its middle is in a gangrenous condition; at the proximal and distal portions beginning necrotic changes are observed.

FIG. 3.—Acute perforative appendicitis.

FIG. 4.—The same, showing gangrene of the entire mucous membrane lining the organ.

[1] These colored sketches were made by the artist from the fresh specimens immediately after removal.